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## Attachment A

APPLICANT FACSIMILE OF FORM PTC-1440  
REV 7-80U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE

ATTY DOCKET NO.

BBI-009C4CN

SERIAL NO.

09/241,347

LIST OF PUBLICATIONS CITED BY APPLICANT  
(Use several sheets if necessary)APPLICANT  
Hermann Buiard and Manfred Gossen  
FILING DATE  
February 2, 1995GROUP  
1632

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
AA	5,221,778	6/93	Byrne et al.	800	2	
AB	4,833,080	05/89	Brent et al.	435	172.3	

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
AC	WO 94/04672	03/94	PCT			
AD	WO 92/20808	11/92	PCT			
AE	WO 91/19784	12/91	PCT			
AF	WO 93/04169	03/93	PCT			
AG	WO 91/19796	12/91	PCT			
AH	WO 92/11874	07/92	PCT			
AI	EP 0 332 416	09/89	EPO			
AJ	WO 93/23431	11/93	PCT			
AK	WO 94/18317	08/94	PCT			
AL	0 455 687 B1	11/91	EPO			
AM	0 455 424 A2	11/91	EPO			
AN	0 494 724 A2	07/92	EPO			

## OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

AO	Hinrichs, W., et al., (1994) "Structure of the Tet Repressor-Tetracycline Complex and Regulation of Antibiotic Resistance", <i>Science</i> , Vol. 264, pp. 418-420;
AO'	Hecht, B., et al., (1993) "Noninducible Tet Repressor Mutations Map from the Operator Motif to the C Terminus", <i>Journal of Bacteriology</i> , Vol. 175, No. 4;
AP	Gossen, M., et al., (1993) "Control of gene activity in higher eukaryotic cells by prokaryotic regulatory elements", <i>TIBS</i> , Vol. 18, No. 12, pp. 471-475;
AQ	Fieck, A., et al., (1992) "Modification of the <i>E. Coli</i> Lac Repressor for Expression in Eukaryotic Cells: Effect of Nuclear Signal Sequence on Protein Activity and Nuclear Documentation", <i>Nucleic Acid Research</i> , Vol. 20, pp. 1785-1791;
AR	Seipel, K., et al., (1992) "Different activation domains stimulate transcription from remote ('enhancer') and proximal ('promoter') positions", <i>The EMBO Journal</i> , Vol. 11, No. 13, pp. 4961-4968;
AS	Epstein-Baak, R., et al., (1992) "Inducible Transformation of Cells from Transgenic Mice Expressing SV40 under Lac Operon Control", <i>Cell Growth &amp; Differentiation</i> , Vol. 3, pp. 127-134;
AT	Gossen, M., and Bujard, H., (1992) "Tight control of gene expression in mammalian cells by tetracycline-responsive promoters", <i>Proceedings of the National Academy of Science</i> , Vol. 89, pp. 5547-5551;
AU	Bradley, A., (1991) "Modifying the mammalian genome by gene targeting", <i>Current Opinion in Biotechnology</i> , Vol. 2, pp. 832-829;
AV	Wyborski, D.L., and Short, J.M., (1991) "Analysis of Inducers of the <i>E. Coli</i> Lac Repressor System in Mammalian Cells and Whole Animals", <i>Nucleic Acid Research</i> , Vol. 19, pp. 4647-4653;

Examiner

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Date Considered

7/9/01

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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LIST OF PUBLICATIONS CITED BY APPLICANT  
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## OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

BA	Degenkolb, J., et al., (1991) "Structural Requirements of Tetracycline-Tet Repressor Interaction: Determination of Equilibrium Binding Constants for Tetracycline Analogs with the Tet Repressor", <i>Antimicrobial Agents and Chemotherapy</i> , Vol. 35, No. 8, pp. 1591-1595;
BB	Baim, S.B., et al., (1991) "A chimeric mammalian transactivator based on the <i>lac</i> repressor that is regulated by temperature and isopropyl $\beta$ -D-thiogalactopyranoside", <i>Proceedings of the National Academy of Science</i> , Vol. 88, pp. 5072-5076;
BC	Gatz, C., et al., (1991) "Regulation of a modified CaMV 35S promoter by the Tn 10-encoder Tet receptor in transgenic tobacco", <i>Mol. Gen. Genet.</i> , Vol. 227, No. 2, pp. 229-237;
BD	Wissmann, A., et al., (1991) "Selection for Tn10 Tet Repressor Binding to tet Operator in <i>Escherichia coli</i> : Isolation of Temperature-Sensitive Mutants and Combinatorial Mutagenesis in the DNA Binding Motif", <i>Genetics</i> , Vol. 128, pp. 225-232;
BE	Labow, M.A., et al., (1990) "Conversion of the <i>lac</i> Repressor into an Allosterically Regulated Transcriptional Activator for Mammalian Cells", <i>Molecular and Cellular Biology</i> , Vol. 10, No. 7, pp. 3343-3356;
BF	Deuschle, U., et al., (1989) "Regulated expression of foreign genes in mammalian cells under the control of coliphage T3 RNA polymerase and <i>lac</i> repressor", <i>Proceedings of the National Academy of Science</i> , Vol. 86, pp. 5400-5404;
BG	Capecci, M.R., (1989) "Altering the Genome by Homologous Recombination", <i>Science</i> , Vol. 244, pp. 1288-1292;
BH	Mermod, N., et al., (1989) "The Proline-Rich Transcriptional Activator of CTF/NF-I Is Distinct from the Replication and DNA Binding Domain", <i>Cell</i> , Vol. 58, 741-753;
BI	Mansour, S.L., et al., (1988) "Disruption of the proto-oncogene <i>int-2</i> in mouse embryo-derived stem cells: a general strategy for targeting mutations to non-selectable genes", <i>Nature</i> , Vol. 336, pp. 348-352;
BJ	Gatz, C., and Quail, P.H., (1988) "Tn10-encoded <i>tet</i> repressor can regulate an operator-containing plant promoter", <i>Proceedings of the National Academy of Science</i> , Vol. 85, pp. 1394-1397;
BK	Figge, J., et al., (1988) "Stringent Regulation of Stably Integrated Chloramphenicol Acetyl Transferase Genes by <i>E. coli</i> <i>lac</i> Repressor in Monkey Cells", <i>Cell</i> , Vol. 52, 713-722;
BL	Triebenberg, S.J., et al., (1988) "Functional dissection of VP16, the <i>trans</i> -activator of herpes simplex virus immediate early gene expression", <i>Genes &amp; Development</i> , Vol. 2, pp. 718-729;
BM	Courey, A.J., and Tjian, R., (1988) "Analysis of Sp1 <i>In Vivo</i> Reveals Multiple Transcriptional Domains, Including a Novel Glutamine-Rich Activation Motif", <i>Cell</i> , Vol. 55, pp. 887-898;
BN	Tovar, K., et al., (1988) "Identification and nucleotide sequence of the class E <i>tet</i> regulatory elements and operator and inducer binding of the encoded purified Tet repressor", <i>Mol. Gen. Genet.</i> , Vol. 215, pp. 76-80;
BO	Altschmied, L., et al., (1988) "A threonine to alanine exchange at position 40 of Tet repressor alters the recognition of the sixth base pair of <i>tet</i> operator from GC to AT", <i>The EMBO Journal</i> , Vol. 7, No. 12, pp. 4011-4017;
BP	Brown, M., et al., (1987) "lac Repressor Can Regulate Expression from a Hybrid SV40 Early Promoter Containing a <i>lac</i> Operator in Animal Cells", <i>Cell</i> , Vol. 49, pp. 603-612;
BQ	Hu, M.-C.-T and Davidson, N., (1987) "The Inducible <i>lac</i> Operator-Repressor System Is Functional in Mammalian Cells", <i>Cell</i> , Vol. 46, pp. 555-566;
BR	Smithies, O., et al., (1985) "Insertion of DNA sequences into the human chromosomal $\beta$ -globin locus by homologous recombination", <i>Nature</i> , Vol. 317, pp. 230-234;
BS	Boshart, M., et al., (1985) "A Very Strong Enhancer Is Located Upstream of an Immediate Early Gene of Human Cytomegalovirus", <i>Cell</i> , Vol. 41, No. 2, pp. 521-530;
BT	Postle, K., et al., (1984) "Nucleotide sequence of the repressor gene of the TN10 tetracycline resistance determinant", <i>Nucleic Acid Research</i> , Vol. 12, No. 12, pp. 4849-4863;
BU	Unger, B., et al., (1984) "Nucleotide sequence of the gene, protein purification and characterization of the pSC101-encoded tetracycline resistance-gene-repressor", <i>Gene</i> , Vol. 31, pp. 103-108;

Examiner

Date Considered

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\*EXAMINER:

Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY DOCKET NO. <b>BBI-009C4CN</b>	SERIAL NO. <b>09/241,347</b>
<b>LIST OF PUBLICATIONS CITED BY APPLICANT</b> (Use several sheets if necessary)		APPLICANT <b>Hermann Bujard and Manfred Gossen</b>	FILING DATE <b>February 2, 1995</b>
<b>COPY</b>			

**OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)**

CA	Unger, B., et al., (1984) "Nucleotide sequence of the repressor gene of the RA1 tetracycline resistance determinant: structural and functional comparison with three related Tet repressor genes", <i>Nucleic Acid Research</i> , Vol. 12, No. 20, pp. 7693-7703;
CB	Waters, S.H, et al. (1983) "The tetracycline resistance determinants of RP1 and Tn1721: nucleotide sequence analysis", <i>Nucleic Acid Research</i> , Vol. 11, No. 17, pp. 6089-6105;
CC	Hillen, W., and Schollmeier, K., (1983) "Nucleotide sequence of the Tn10 encoded tetracycline resistance gene", <i>Nucleic Acid Research</i> , Vol. 11, No. 2, pp. 525-539;
CD	Brent, R. and M. Ptashne (1984) "A Bacterial Repressor Protein or a Yeast Transcriptional Terinator Can Block Upstream Activation of A Yeast Gene" <i>Nature</i> 312:612-615;
CE	Brent R. and M. Ptashne (1985) "A Eukaryotic Transcriptional Activator Bearing the DNA Specificity of a Prokaryotic Repressor" <i>Cell</i> 43:729-736;
CF	Baniahmad, A. et al. (1992) "A Transferable Silencing Domain Is Present In the Thyroid Hormone Receptor, In the v-erbA Oncogene Product and In the Retinoic Acid Receptor" <i>The EMBO Journal</i> 11(3):1015-1023;
CG	Sauer, F. and H. Jäckle (1993) "Dimerization and the Control of Transcription by Krüppel" <i>Nature</i> 364:454-457;
CH	Licht, J. et al. (1990) "Drosophila Krüppel Protein is a Transcriptional Repressor" <i>Nature</i> 346:76-79;
CI	Herschbach B. and A. Johnson (1993) "Transcriptional Repression In Eukaryotes" <i>Annu. Rev. Cell Biol.</i> 9:479-509;
CJ	Renkawitz R. (1990) "Transcriptional Repression In Eukaryotes" <i>TIG</i> 6(6):192-193;
CK	Resnitzky D. (1994) "Acceleration of the G1/S Phase Transition by Expression of Cyclins D1 and E with an Inducible System" <i>Molecular and Cellular Biology</i> 14(3):1669-1679;
CL	Furth P. (1994) "Temporal Control of Gene Expression in Transgenic Mice By A Tetracycline-Responsive Promoter" <i>Proc. Natl. Acad. Sci. USA</i> 91:9302-9306;
CM	Wimmel A. et al. (1994) "Inducible Acceleration of G1 Progression Through Tetracycline-Regulated Expression of Human Cyclin E" <i>Oncogene</i> 9:995-997
CN	Ackland-Berglund, C.E. and Leib, D.A.. (1995) "Efficacy of Tetracycline-Controlled Gene Expression Is Influenced by Cell Type" <i>BioTechniques</i> 18(2):196-200;
CO	Gossen M. and B. Hermann (1993) "Anhydrotetracycline, A Novel Effector of Tetracycline Controlled Gene Expression Systems In Eukaryotic Cells" <i>Nucleic Acids Research</i> 21(18):4411-4412;
CP	Buckbinder L. et al. (1994) "Gene Regulation by Temperature-Sensitive p53 Mutants: Identification of p53 response genes" <i>Proc. Natl. Acad. Sci. USA</i> 91:10640-10644;
CQ	Yarranton G. (1992) "Inducible Vectors For Expression In Mamalian Cells" <i>Current Opinion in Biotechnology</i> 3:506-511;
CR	Gossen et al. (1994) "Inducible Gene Expression Systems For Higher Eukaryotic Cells" <i>Current Opinion in Biotechnology</i> 5:516-520;
CS	Weinmann P. et al. (1994) "A Chimeric Transactivator Allows Tetracycline-Responsive Gene Expression in Whole Plants" <i>The Plant Journal</i> 5(4):559-569;
CT	Pescini R. et al. (1994) "Inducible Inhibition of Eukaryotic Gene Expression" <i>Biochemical and Biophysical Research Communications</i> 202(3):1664-1667;
CU	Fishman G. et al. (1994) "Tetracycline-Regulated Cardiac Gene Expression in Vivo" <i>J. Clin. Invest.</i> 93:1864-1868;

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## U.S. PATENT DOCUMENTS

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## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
	AB	WO 94/29442	12/94	PCT			

## OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

AC	Cowell, "Repression versus activation in the control of gene transcription," <i>Trends in Biochemical Sciences</i> , 19:1, 38-42 (1994);
AD	Deuschle et al., "Tetracycline-reversible silencing of eukaryotic promoters," <i>Mol. Cell. Biol.</i> , 15:4, 1907-1914 (1995);
AE	Gatz et al., "Stringent repression and homogeneous de-repression by tetracycline of a modified CaMV 35S promoter in intact transgenic tobacco plants," <i>The Plant Journal</i> , 2:3, 397-404 (1992);
AF	Gossen et al., "Exploiting prokaryotic elements for the control of gene activity in higher eukaryotes," Keystone Symposium on Gene Therapy and Molecular Medicine, Steamboat Springs, Colorado, <i>Journal of Cellular Biochemistry</i> , Supplement 0 (21A), Abstract no. C6-220, 355 (1995);
AG	Gossen et al., "Transcriptional activation by tetracyclines in mammalian cells," <i>Science</i> , 268:5218, 1766-1769 (1995);
AH	Liang et al., "Enhanced and switchable expression systems for gene-transfer," Keystone Symposium on Gene Therapy and Molecular Medicine, Steamboat Springs, Colorado, <i>Journal of Cellular Biochemistry</i> , Supplement 0 (21A), Abstract no. C6-220, 379 (1995).
AI	Agarwal, M.L. et al., "p53 Controls Both the G <sub>2</sub> /M and the G <sub>1</sub> Cell Cycle Checkpoints and Mediates Reversible Growth Arrest in Human fibroblasts," <i>Proc. Natl. Acad. Sci. USA</i> , 92: pp. 8493-8497 (1995);
AJ	Bergman, M. et al. "Overexpressed Csk Tyrosine Kinase Is Localized in Focal Adhesions, Causes Reorganization of $\alpha\beta$ Integrin, and Interferes with HeLa Cell Spreading", <i>Molecular and Cellular Biology</i> , 15, No. 2, pp. 711-722 (1995);
AK	Cayrol, C. et al. "Identification of Cellular Target Genes of the Epstein-Barr Virus Transactivator Zta: Activation of Transforming Growth Factor $\beta$ igh3 (TGF- $\beta$ igh3) and TGF- $\beta$ 1", <i>Journal of Virology</i> , 69, No. 7, pp. 4206-4212, (1995);
AL	Chen, Y.Q. et al. "Tumor Suppression by p21WAF11", <i>Cancer Research</i> , 55, pp. 4536-4539, (1995);
AM	Dhawan, J. et al. "Tetracycline-Regulated Gene Expression Following Direct Gene Transfer into Mouse Skeletal Muscle", <i>Somatic Cell and Molecular Genetics</i> , 21, No. 4, pp. 233-240, (1995);
Examiner	RAS
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							YES NO

## OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

AN	Efrat, S. et al. "Conditional Transformation of a Pancreatic $\beta$ -Cell Line Derived From Transgenic Mice Expressing A Tetracycline-Regulated Oncogene" <i>Proc. Natl. Acad. Sci. USA</i> , 92, pp. 3576-3580 (1995);
AO	Gjetting, T. et al. "Regulated Expression of the Retinoblastoma Susceptibility Gene in Mammary Carcinoma Cells Restores Cyclin D1 Expression and G <sub>1</sub> -Phase Control", <i>Biol. Chem. Hoppe-Seyler</i> , 376, pp. 441-446 (1995);
AP	Haase, S.B. et al. "Transcription Inhibits the Replication of Autonomously Replicating Plasmids in Human Cells", <i>Molecular and Cellular Biology</i> , 14, No. 4, pp. 2516-2524 (1994);
AQ	Hennighausen, L. et al. "Conditional Gene Expression in Secretory Tissues and Skin of Transgenic Mice Using the MMTV-LTR and the Tetracycline Responsive System", <i>Journal of Cellular Biochemistry</i> , 59, pp. 463-472, (1995);
AR	Howe, J.R. et al. "The Responsiveness of a Tetracycline-Sensitive Expression System Differs in Different Cell Lines", <i>The Journal of Biological Chemistry</i> , 270, No. 23, pp. 14168-14174, (1995);
AS	Miller, K. et al. "The Function of Inducible Promoter Systems in F9 Embryonal Carcinoma Cells", <i>Experimental Cell Research</i> , 218, pp. 144-150, (1995);
AT	Passman, R.S. et al., "Regulated Expression of Foreign Genes In Vivo After Germline Transfer", <i>J. Clin. Invest.</i> , 94, pp. 2421-2425 (1994)
AU	Sopher, B.L. et al., "Cytotoxicity Mediated By Conditional Expression of a Carboxyl-Terminal Derivative of the $\beta$ -Amyloid Precursor Protein", <i>Molecular Brain Research</i> , 26, pp. 207-217, (1994);
AV	Wu, Z. et al. "Conditional Ectopic Expression of C/EBP $\beta$ in NIH-3T3 Cells Induces PPAR $\gamma$ and Stimulates Adipogenesis", <i>Genes &amp; Development</i> , 9, pp. 2350-2363, (1995).

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